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Emergency department utilization and subsequent prescription drug overdose death

Joanne E. Brady, PhD^{a,b,c,*}, Charles J. DiMaggio, PhD^d, Katherine M. Keyes, PhD^{b,c}, John J. Doyle, DrPH^b, Lynne D. Richardson, MD^e, and Guohua Li, MD, DrPH^{a,b,c}

^aDepartment of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, NY

^bDepartment of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY

^cCenter for Injury Epidemiology and Prevention, Columbia University Medical Center, New York, NY

^dDepartment of Surgery, New York University School of Medicine, New York, NY

^eDepartment of Emergency Medicine, Mount Sinai School of Medicine, New York, NY

Abstract

Purpose—Prescription drug overdose (PDO) deaths are a critical public health problem in the United States. This study aims to assess the association between emergency department (ED) utilization patterns in a cohort of ED patients and the risk of subsequent unintentional PDO mortality.

Methods—Using data from the New York Statewide Planning and Research Cooperative System for 2006–2010, a nested case-control design was used to examine the relationship between ED utilization patterns in New York State residents of age 18–64 years and subsequent PDO death.

Results—The study sample consisted of 2732 case patients who died of PDO and 2732 control ED patients who were selected through incidence density sampling. With adjustment for demographic characteristics, and diagnoses of pain, substance abuse, and psychiatric disorders, the estimated odds ratios of PDO death relative to one ED visit or less in the previous year were 4.90 (95% confidence interval [CI]: 4.50–5.34) for those with two ED visits, 16.61 (95% CI: 14.72–18.75) for those with three ED visits, and 48.24 (95% CI: 43.23–53.83) for those with four ED visits or more.

Conclusions—Frequency of ED visits is strongly associated with the risk of subsequent PDO death. Intervention programs targeting frequent ED users are warranted to reduce PDO mortality.

Keywords

Drug overdose; Emergency service, hospital; Prescription drugs; Prevention and control

*Corresponding author. Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 West 168th Street, 5th Fl, New York, NY 10032. Tel.: +1-212-305-9518. jobrady@gmail.com (J.E. Brady).

Introduction

Increases in drug overdose death in the United States are a critical public health problem. Nearly 60% of drug overdose deaths involved prescription drugs, and in 2011, 1.4 million emergency department (ED) visits involved nonmedical use of prescription drugs [1,2]. Frequent ED utilization has been shown to be a marker for substance use—narcotic use, especially [3,4], and is associated with nonmedical opioid use, drug diversion, and poorly controlled pain [3–5]. Therefore, frequent ED utilization may be a marker for increased risk for prescription drug overdose (PDO), and this point of clinician contact may serve as a setting to launch preventive intervention efforts [6–15]. Preventive interventions targeted at ED patients at high risk for PDO death, may include advice such as not mixing opioids with sedatives or alcohol [16], or targeted patient education initiatives [17]. Furthermore, identifying high risk populations can help medical practitioners decide whom to target with screening, intervention (e.g., take-home naloxone), and treatment program referrals [18–24].

Despite the importance of the ED as a key clinical entry point for patients at high risk of PDO, the relationship between ED utilization patterns and subsequent drug overdose death is understudied. In the present study, we used a nested case-control design to examine the relationship between ED utilization in a cohort of ED patients and the risk of subsequent unintentional PDO death. Characterizing risk markers for fatal PDO available in administrative databases can be useful for identifying individuals at increased likelihood of PDO death. The goal of the analysis was to determine whether increased ED utilization in a cohort of ED patients was associated with subsequent unintentional PDO death.

Materials and methods

Data sources

Data for this study came from the New York Statewide Planning and Research Cooperative System (SPARCS) for the years 2006–2010. SPARCS is a data reporting system that collects ED visit data from nonfederal hospitals in New York State (NYS) [25]. SPARCS contains patient-level data including patient characteristics, discharge diagnoses, procedures received, and charges for ED visits [25]. To ensure data quality, SPARCS visit data are examined for proper formatting upon submission format [26]. Data completeness and accuracy are assessed for each facility. Data are reviewed monthly and compared with other benchmarks from Department of Health data [26,27]. To ascertain dates of death, and underlying and contributing causes of death for patients who visited the ED during the study period, SPARCS ED data were linked to NYS and New York City vital statistics records by a SPARCS analyst. Data were linked based on the patient's date of birth, residential address, first two characters of the patient's first name, the first and last two characters of the patient's last name, and the last four digits of the patient's social security number. PDO mortality within one year of the most recent ED visit within the study period 2006–2010 was evaluated. The study protocol was reviewed and approved by the Institutional Review Board of Columbia University Medical Center (IRB-AAAK6304 New York, NY).

ED utilization

ED utilization (1, 2, 3, and 4 visits) in last year of follow-up was calculated with respect to date of death for cases. The choice of these time frames was based on research by the Agency for Healthcare Research and Quality, which proposed two ED visits or more in 3 days, three ED visits or more in 90 days, and four ED visits or more in a year as metrics to track suboptimal quality of care [28].

Model evaluation for which ED utilization time frame best fit the data was based on Akaike information criterion statistics [29]. Time-varying 365-day ED utilization was operationalized using three separate indicator variables: two, three, or four or more ED visits in a 365-day time window. When calculating these ED utilization measures, admissions for patients who were transferred on the day of discharge to other acute care hospitals, including patients admitted to hospital specialty units, inpatient rehabilitation facilities, skilled nursing facilities, and long-term care hospitals, were collapsed and treated as one continuous admission. If a patient died at the ED, this visit was not counted. Same-day ED revisits were included in the analyses.

Other risk markers

Other risk markers that were evaluated included age, sex, and race (white, black, Asian/Pacific Islander/Native American, and other). To help improve model fit, a discharge against medical advice (AMA) at the initial ED visit and several other diagnoses were examined as potential risk markers for drug overdose death given that discharges AMA are associated with drug abuse [30]. Previous studies have noted a rise in nontraumatic dental condition-related ED visits that may result in an opioid analgesic prescription (Online Appendix A) [31–33]. Studies of drug overdose have noted that substance use disorders, mental health disorders, and chronic pain conditions are associated with drug overdose [34–42]. Accordingly, these conditions were evaluated as potential risk markers of PDO death. In accordance with the State Personal Privacy Protection Law, individual characteristics involving less than six patients may not be reported.

Outcome measurements

Classification codes from the *International Classification of Diseases and Related Health Problems, 10th Revision* were used to classify PDO deaths. Unintentional and undetermined intent overdose deaths (X40–X44, Y10–Y14), where there was also an indication that a prescription drug was a contributing cause of death (T40.2, T40.3, T40.4 [opioid analgesics], T40.6 [Other and unspecified narcotics], T42.2 [Succinimides and oxazolindiones], T42.3 [Barbiturates], T42.4 [Benzodiazepines], T43.0 [Tricyclic and tetracyclic antidepressants], T43.1 [Monoamine-oxidase-inhibitor antidepressants], T43.2 [other and unspecified antidepressants], T50.9 [other and unspecified drugs]), were evaluated as the primary outcome of interest [43,44].

Study design

A nested case-control study design was used. ED patients who subsequently died of PDO during the follow-up were considered cases. Using incidence density sampling, one control

was randomly selected from the same base population from which the cases arose and was matched to the corresponding case on follow-up time [45]. The first visit date in the study period was considered the entry visit. The end of follow-up for cases was the date when PDO death occurred. For controls, the end of follow-up time corresponded to elapsed time from study entry to the time when death occurred for the matched case. To be eligible to be a control the individual must be alive when the case occurred. All case patients were able to be matched with control patients. Incidence density sampling was used because ED utilization is time-varying. Time-dependent covariates may be accurately assessed in nested case-control study by using incidence density-based sampling to create risk sets [45].

The cohort from which the cases arose included patients who were NYS residents, were 18–64 years of age, and who visited the ED in NYS from 2006–2010 (Fig. 1). Patients with any discharge diagnoses indicating palliative care, cancer, metastatic carcinoma, or sickle cell anemia at any ED visit were excluded from the cohort because they may have different ED utilization patterns and may receive higher doses of opioids than other patients. Patients without a previous ED visit who died during the index ED visit were excluded from the cohort because there was no pattern of prior ED visits to predict the study outcome. Of the remaining patients who visited the ED, all individuals who subsequently died of a PDO death were used as cases.

Statistical analysis

To better understand the attributes of the individuals included in this study, the frequency distribution of patient characteristics at the initial ED visit from 2006–2010 who subsequently died of a PDO was compared with those of patients who did not. Differences between groups were compared using χ^2 tests. A *P*-value of .05 or less was considered statistically significant. Baseline characteristics were examined in unadjusted models to estimate the odds ratio (OR) and 95% confidence interval (CI) for PDO death. Conditional logistic regression was used to estimate ORs [46,47]. Because this study is based on the nested case-control design, the measure of association is the OR. With incidence density sampling, the OR approximates the incidence rate ratio [48]. To prevent over-adjustment in multivariable models, demographic characteristics (age, sex, and composite independent variables of diagnoses at study entry) were created and included in the final multivariable model. Four binary composite independent variables of diagnoses at entry were created, including presence or absence of the following: (1) Diagnosis of alcohol abuse, alcohol drug seeking, drug dependence, opioid abuse, other drug abuse, nonfatal opioid overdose, or sedative anxiolytic abuse at the initial ED visit; (2) Diagnosis of anxiety disorder, depression, episodic mood disorder, major depressive disorder, personality disorder, post-traumatic stress disorder, psychosis or agitation, or schizophrenia at their initial ED visit; (3) Diagnosis of back pain, fibromyalgia, or musculoskeletal pain at their initial ED visit; (4) Diagnosis of general symptoms, soft tissue disorders, nontraumatic dental conditions, or vertebrae disorders at their initial ED visit. The multivariable models included the following independent variables: time independent age at study entry, sex, race, AMA status, composite independent variables of diagnoses at study entry, and time-varying ED utilization. Analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

A total of 2732 PDO deaths were recorded during the follow-up and were used as cases in this study (Fig. 1). Characteristics of cases and controls at study entry showed that patients who subsequently died of a PDO were disproportionately 35–54 years of age (59.1% vs. 42.2%, $\chi^2 = 170.5$, $P < .0001$), male (65.2% vs. 44.2%, $\chi^2 = 243.3$, $P < .0001$), and identified as white race (74.4% vs. 51.6%, $\chi^2 = 319.3$, $P < .0001$) compared with patients that did not die of PDO (Table 1). Additionally, patients who subsequently died of a PDO were more likely to be discharged AMA at the initial visit (3.9% vs. 2.1%, $\chi^2 = 15.2$, $P < .0001$, Table 1) than those that did not die. In unadjusted models, patients who were discharged AMA at the initial ED visit were more likely to subsequently die of PDO (Table 2) than patients were not discharged AMA. Having a psychiatric disorder diagnosis, or any substance abuse, or dependence diagnosis was also associated with increased risk of PDO death (Table 2).

Multivariable models adjusted for age, race, and sex show that drug, or alcohol abuse, or dependence diagnoses at an initial ED visit were associated with five times greater risk of PDO death (adjusted odds ratio [aOR]: 5.40, 95% CI: 4.84–6.03, Table 3). Having a psychiatric disorder diagnosis at the initial ED visit was associated with a three times higher risk of subsequent PDO death compared with patients without a psychiatric disorder diagnoses at the initial ED visit (aOR: 3.71, 95% CI: 3.23–4.14). Having a pain-related diagnosis at the initial ED visit was associated with a 73% higher risk of PDO death (aOR: 1.88, 95% CI: 1.60–1.86). Other diagnoses, including general symptoms, soft tissue, nontraumatic dental, or vertebrae disorders at an initial ED visit were associated with 40% higher risk of PDO death (aOR 1.38, 95% CI 1.28–1.63). A discharge AMA at the initial visit was also associated with subsequent PDO death (aOR: 1.38, 95% CI: 1.16–1.58).

At the end of follow-up, about 50% of the cases and 15% of the controls had two or more visits in the prior year. Relative to one or less visit in the previous year, the aORs of PDO death were 4.90 (95% CI: 4.50–5.34) for those with two visits, 16.61 (95% CI: 14.72–18.75) for those with three visits, and 48.24 (95% CI: 43.23–53.83) for those with four or more visits (Table 3).

Discussion

This study is among one of the first studies to evaluate the relationship between patterns of ED utilization and PDO death, as opposed to the more well-defined literature on “doctor shopping,” the practice of visiting multiple health care providers to obtain controlled substances [49–53]. ED utilization patterns are thought to be related to poorly controlled pain and in some instances substance use [3,54,55]. This study indicates that ED utilization patterns are also important predictors of PDO death.

ED visits are common among people who abuse drugs and alcohol [6,56–58]. An alcohol intervention trial of college students found that 30% of men and 27% women visited the ED at least once in the 2 years of follow-up [6]. Another study of adolescents using ED at the University of Michigan Medical Center found that 35% of past-year self-reported nonmedical prescription opioid users had an ED visit in the prior year, compared with 25%

of respondents not reporting past-year nonmedical prescription opioid users [58]. Compared with individuals not reporting past-year nonmedical sedative use, self-reported past-year nonmedical sedative users were more likely to have had an ED visit in the past year (25% vs. 40%) [58].

Additionally, this investigation demonstrates that patients who were discharged AMA were more likely to die of PDO death than patients who were not discharged AMA; previous literature has shown that leaving AMA is associated with substance use [30]. Although it is generally believed that drug-seeking patients have increased ED utilization and that patients discharged AMA are more likely to abuse drugs and alcohol, examination of ED utilization patterns with respect to overdose is scant [30,54,55].

This study confirms prior findings that patients who are male, ages 35–54 years, and are identified as white race are at increased risk for PDO compared with females, other age groups, and races [34,39,40,43,52,59–63], and it mirrors previous research on the association of clinical risk markers for overdose, such as psychiatric comorbidities, drug and alcohol abuse, previous ED visits for opioid overdose and chronic pain conditions [34–36,39,40,64]. Of note, at study entry, chronic pain and other conditions, such as visceral pain and headaches, which previous studies have found to be frequently occurring in patients who overdose [36,55], were more frequently noted for patients who did not subsequently die of PDO.

ED visits may serve as an opportunity to launch a preventive intervention, as to date findings suggest that prescription drug monitoring programs have had limited or mixed effects on reducing drug overdose deaths and opioid or other controlled substance prescribing [65–69]. Risk assessment and stratification can help identify patients most vulnerable to overdose who are using ED services [40,62]. Based on all 2006–2010 SPARCS ED data, about 40% of patients who subsequently die of overdose, who were 18–64 years, and NYS residents had multiple ED encounters (data not shown). About 19% of people who died of PDO did not visit the ED during the study period (data not shown).

These repeated visits represent opportunities to intervene, such as referral to substance abuse treatment, or access to rescue treatments, including take-home naloxone for reversing opioid overdose. A Canadian study found that by monitoring frequent ED users, it was possible to reduce ED visits and improve patient care by using medical and social interventions, such as denying narcotic and benzodiazepine prescriptions, restricting patients to using one pharmacy, providing supportive counseling, and linking patients with community mental health services [70]. Although there is debate regarding the appropriateness of interventions in already overburdened EDs, reports show that individuals with four ED visits or more in a year make up 28% of all ED visits [28], suggesting interventions targeted at high ED utilizers adequate care outside the ED may help alleviate strain on EDs.

Limitations

This study has several notable limitations. First, this study examines whether ED utilization patterns can predict overdose death. Preventive interventions launched in the ED will not directly affect drug user populations who do not use ED services, and only 40% of all

overdose victims 18–64 years of age in NYS had multiple ED visits. If patients who died at their only ED visit had been included, effect estimates would have been slightly attenuated. Second, increased health care utilization is a marker of illness and sicker patients who are more likely to receive more pharmacologic treatments and are at increased risk for all-cause mortality. Third, this investigation is based on currently coded diagnoses and not necessarily conditions present in individuals; some conditions may not be recorded in administrative data. It is likely that only the most severe comorbidities of patients are recorded, and that the findings of this study may not be generalizable to patients with less severe disease. Fourth, this study does not evaluate provider prescribing or its appropriateness. Because SPARCS does not collect prescription drug data, it is not possible to determine if patients were prescribed prescription opioids or other drugs at their ED visit. Similarly, other important characteristics cannot be accounted for such as, drugs taken, drug dosages, the setting in which drugs were taken or the mode of drug administration (e.g., oral or intravenous), factors associated with opioid adverse events, and overdose death [39,60,62,71–73]. Fifth, there have been conflicting studies regarding the accuracy of drug overdose death certification and coding [74–77]. If drug overdose deaths are not ascertained and indiscriminately not recorded on death certificates, this study may underestimate effect estimates. Additionally, if a death to a NYS resident occurred out of state, the death would not be captured in this analysis.

Conclusions

ED utilization patterns are a strong predictor of subsequent overdose death. Understanding the timing of overdose death in relation to ED utilization is essential to recognizing which patients to target with overdose prevention interventions. Identifying markers for increased risk is paramount for optimizing the effectiveness of preventive intervention efforts, such as providing high-risk patients, their friends and families with take-home naloxone, or drug treatment referral. Future studies should focus on identifying other health encounter patterns and alternative approaches to aid vulnerable individuals who do not use ED services.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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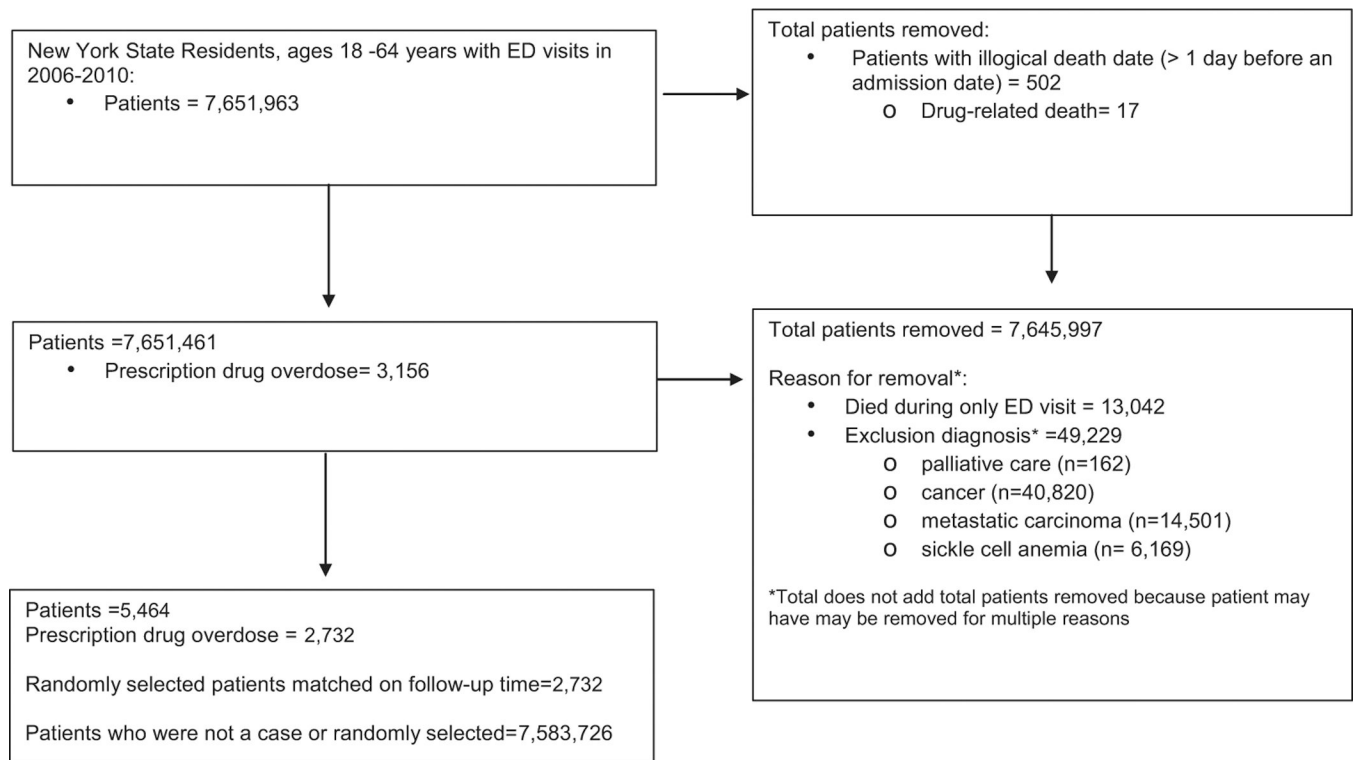


Fig. 1.
Flowchart of ED data study population, New York SPARCS, New York State, 2006–2010.

Table 1

ED utilization and demographic and clinical characteristics by case-control status, SPARCS emergency department data, New York State, 2006–2010

Characteristics*	Cases		Controls	
	No.	%	No.	%
ED visits in the last year of follow-up				
1	1388	50.8	2312	84.6
2	464	17.0	244	8.9
3	278	10.2	81	3.0
4	602	22.0	95	3.5
Demographics				
Age [†] (y)				
18–24	351	12.9	592	21.7
25–34	541	19.8	655	24.0
35–44	796	29.1	596	21.8
45–54	818	29.9	558	20.4
55–64	226	8.3	331	12.1
Sex [†]				
Female	951	34.8	1525	55.8
Male	1781	65.2	1207	44.2
Race [†]				
White	2033	74.4	1410	51.6
Black or African American	313	11.5	679	24.9
Native American/Asian/Pacific Islander	26	1.0	76	2.8
Other or unknown	360	13.2	567	20.8
Clinical characteristics				
Discharged AMA [†]				
Yes	106	3.9	57	2.1
No	2626	96.1	2675	97.9
Psychiatric diagnosis				
Anxiety disorder [†]				
Yes	125	4.6	51	1.9
No	2607	95.4	2681	98.1
Depression [†]				
Yes	125	4.6	35	1.3
No	2607	95.4	2697	98.7
Episodic mood disorder [†]				
Yes	100	3.7	25	0.9
No	2632	96.3	2707	99.1
Major depressive disorder				

Characteristics*	Cases		Controls	
	No.	%	No.	%
Yes	18	0.7	11	0.4
No	2714	99.3	2721	99.6
Personality disorder [†]				
Yes	107	3.9	26	1.0
No	2625	96.1	2706	99.1
Psychosis or agitation [†]				
Yes	95	3.5	12	0.4
No	2637	96.5	2720	99.6
Schizophrenia [†]				
Yes	42	1.5	7	0.3
No	2690	98.5	2725	99.7
Substance use diagnosis				
Alcohol abuse [†]				
Yes	215	7.9	68	2.5
No	2517	92.1	2664	97.5
Alcohol drug seeking [†]				
Yes	486	17.8	97	3.6
No	2246	82.2	2635	96.4
Drug dependence [†]				
Yes	125	4.6	13	0.5
No	2607	95.4	2719	99.5
Opioid abuse [†]				
Yes	48	1.8	7	0.3
No	2684	98.2	2725	99.7
Other drug abuse [†]				
Yes	137	5.0	12	0.4
No	2595	95.0	2720	99.6
Tobacco use disorder [†]				
Yes	104	3.8	69	2.5
No	2628	96.2	2663	97.5
Pain-related diagnosis				
Arthritis				
Yes	99	3.6	88	3.2
No	2633	96.4	2644	96.8
Back pain [†]				
Yes	244	8.9	134	4.9
No	2488	91.1	2598	95.1
Fibromyalgia				
Yes	30	1.1	26	1.0

Characteristics [*]	Cases		Controls	
	No.	%	No.	%
No	2702	98.9	2706	99.1
Headaches				
Yes	73	2.7	92	3.4
No	2659	97.3	2640	96.6
Joint disorder				
Yes	78	2.9	69	2.5
No	2654	97.1	2663	97.5
Musculoskeletal pain				
Yes	306	11.2	301	11.0
No	2426	88.8	2431	89.0
Neuropathy				
Yes	8	0.3	10	0.4
No	2724	99.7	2722	99.6
Visceral pain [†]				
Yes	24	0.9	66	2.4
No	2708	99.1	2666	97.6
Other conditions				
Abdominal symptoms [†]				
Yes	132	4.8	170	6.2
No	2600	95.2	2562	93.8
General symptoms [†]				
Yes	189	6.9	146	5.3
No	2543	93.1	2586	94.7
Nontraumatic dental				
Yes	65	2.4	65	2.4
No	2667	97.6	2667	97.6
Respiratory symptoms [†]				
Yes	135	4.9	204	7.5
No	2597	95.1	2528	92.5
Soft tissue disorder				
Yes	94	3.4	79	2.9
No	2638	96.6	2653	97.1

^{*} Data for prior nonfatal opioid overdose, sedative abuse, post-traumatic stress disorder, central sleep apnea, vertebrae disorders not shown because cell counts less than 6.

[†] $P < 0.05$.

Table 2

Unadjusted ORs and 95% CIs for risk of PDO death by ED utilization and demographic and clinical characteristics from nested case-control analysis, SPARCS ED data, New York State, 2006–2010

Characteristics	OR (95% CI)
ED visits in the past year	
1	
2	3.2 (2.7–3.7)
3	5.7 (4.4–7.4)
4	10.6 (8.4–13.2)
Demographics	
Age (y)	
18–24	0.63 (0.60–0.67)
25–34	1.00
35–44	2.26 (2.15–2.37)
45–54	1.74 (1.65–1.83)
55–64	0.69 (0.65–0.74)
Sex	
Female	1.00
Male	2.01 (1.94–2.08)
Race	
White	1.00
Black or African American	0.29 (0.27–0.30)
Native American/Asian/Pacific Islander	0.27 (0.23–0.31)
Other or unknown	0.47 (0.45–0.50)
Clinical characteristics	
Discharged AMA	2.89 (2.74–3.04)
Psychiatric diagnoses	
Anxiety disorder	4.16 (3.72–4.64)
Depression	2.82 (2.54–3.14)
Episodic mood disorder	4.27 (3.70–4.91)
Major depressive disorder	1.60 (1.26–2.04)
Personality disorder	4.76 (2.8–8.04)
Post-traumatic stress disorder	2.91 (1.81–4.67)
Psychosis or agitation	7.25 (5.99–8.78)
Schizophrenia	5.18 (4.07–6.59)
Substance use diagnoses	
Alcohol abuse	3.23 (2.96–3.51)
Alcohol drug seeking	5.03 (4.68–5.39)
Drug dependence	8.63 (7.16–10.41)
Opioid abuse	13.71 (10.13–18.55)
Other drug abuse	6.81 (5.86–7.93)
Prior nonfatal opioid overdose	13.40 (7.93–22.64)

Characteristics	OR (95% CI)
Sedative anxiolytic abuse	8.57 (5.02–14.61)
Tobacco use disorder	1.46 (1.33–1.61)
Pain-related diagnoses	
Arthritis	1.02 (0.94–1.12)
Back pain	2.20 (2.06–2.35)
Fibromyalgia	1.34 (1.10–1.62)
Headaches	0.98 (0.89–1.07)
Joint disorder	1.09 (0.99–1.22)
Musculoskeletal pain	1.15 (1.09–1.21)
Neuropathy	0.64 (0.48–0.86)
Visceral pain	0.39 (0.33–0.45)
Other conditions	
Abdominal symptoms	0.89 (0.83–0.95)
Central sleep apnea	0.18 (0.05–0.60)
General symptoms	1.09 (1.02–1.17)
Nontraumatic dental	1.13 (1.02–1.26)
Respiratory symptoms	0.72 (0.67–0.77)
Soft tissue disorder	1.38 (1.25–1.51)
Vertebrae disorders	2.22 (1.78–2.78)

Table 3

Adjusted ORs and 95% CIs for risk of PDO death by ED utilization, demographic and clinical characteristics, SPARCS ED data, New York State, 2006–2010

Characteristic	OR (95% CI)
ED visits in the past year	
2	4.90 (4.50–5.34)
3	16.61 (14.72–18.75)
4	48.24 (43.23–53.83)
Age, y	
18–24	0.49 (0.44–0.54)
35–44	1.86 (1.71–2.01)
45–54	1.74 (1.60–1.90)
55–64	0.82 (0.74–0.92)
Race	
Black or African American	0.27 (0.25–0.29)
Native American/Asian/Pacific Islander	0.27 (0.21–0.34)
Other or Unknown	0.42 (0.39–0.45)
Sex	
Male	2.35 (2.22–2.50)
Discharged AMA at initial ED visit	1.38 (1.16–1.63)
Drug or alcohol abuse, or dependence diagnosis	5.40 (4.84–6.03)
Mental health diagnosis	3.71 (3.23–4.14)
Pain-related diagnosis	1.73 (1.60–1.86)
Other diagnosis	1.38 (1.26–1.50)